UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,613	02/29/2000	DEBORAH C. MASH	N08-002	8931

7590 09/26/2005

COLEMAN SUDOL SAPONE P C
714 COLORADO AVENUE
BRIDGEPORT, CT 06605-1601

EXAMINER	
JIANG, SHAOJIA A	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,613	MASH, DEBORAH C.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-9 and 25-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 4-9, and 25-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SOD

DETAILED ACTION

This Office Action is in response to Applicant's amendment and response filed on July 13, 2005 wherein Claims 1-2, 4-9, and 25-30 have been amended. It is noted that claims 3, 10-24 are cancelled previously.

Currently, claims 1-2, 4-9, and 25-30 are pending in this application and under examination on the merits.

Applicant's remarks filed July 13, 2005 with respect to the rejection of claims 6 and 9 made under 35 U.S.C. 112 first paragraph for lack of enablement for "opioid antagonists" of record stated in the Office Action dated January 12, 2005 have been fully considered and found persuasive to remove the rejection since, as Applicant asserts that:

"The term opioid antagonist is one which is well known in the art and the routineer can readily pick and choose from a number of opioid antagorlists specifically set forth in the specification to combine with noribogaine in treating pain according to the present invention. Indeed, opiate receptors were first described in the 1970's so there has been more than three decades of scientific information and practice related to these receptors and in particular, to opioid (receptor) antagonists. There is no absolutely no undue experimentation which has to be utilized for the routineer to make and use the present invention." (see Applicant's remarks at page 5).

Therefore, the said rejection is withdrawn.

The following is new rejection(s) necessitated by Applicant's amendment filed on July 13, 2005.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-9, and 25-30 as amended now are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's amendment submitted July 13, 2005 with respect to amended claims 1-2, 4-9, and 25-30 has been fully considered but is deemed to insert new matter into the claims since the specification as originally filed does not provide support for "pain treatable with an opioid agonist analgesic". The specification as originally filed as a whole **fails define** what kind of pain to be treated; the original specification merely discloses for example at page 3 that:

"Summary of the Invention

In accordance with the present invention, surprising and unexpected properties of noribogine have been discovered. This compound is known to be a metabolite of ibogaine and is chemically identified as 12-hydroxyibognmine. In particular, noribogaine has been found to be useful as a non-addictive analgesic agent and as a treatment for drug dependency or abuse. Pharmaceutical compositions of noribognine can be combined with one or more known opioid antagorlists to treat addiction such that

withdrawal symptoms are substantially eliminated or, at a minimum, surprisingly reduced. Such compositions are conveniently prepared in limit dose form with one or more unit doses providing a therapeutically effective amount of active ingredient.

In its first aspect, the invention is directed to a method of alleviating pain in a patient by administering systemically noribogaine at a therapeutically effective dosage. In a preferred embodiment, administration is by means of a pharmaceutical composition in which noribogaine is the sole analgesic agent. In patients for whom opioid analgesics are contraindicated, noribogaine is administered systemically in an amount of effective to reduce or eliminate pain in the absence of any concomitant opioid analgesic therapy. In each case, the dosage of noribogaine administered to a patient shoeuld be between 0.1 and 100 mg per kg of body weight and, preferably, between 1 and 30 mg per kg of body weight." (emphasis added).

Thus, **nowhere** is the type of pain to be treated defined in the specification. In particular, the description "in patients for whom opioid analgesics are contraindicated" is merely related to a process of treatment, if patients for whom opioid analgesics are contraindicated, noribogaine is administered systemically alone, instead of being concomitant opioid analgesic therapy to reduce or eliminate pain. This written description is not deemed to define what kind of pain to be treated as claimed now.

Consequently, there is nothing within the instant specification which would lead the artisan in the field to believe that Applicant was in possession of the invention as it is now claimed. See *Vas-Cath Inc. v. Mahurkar*, 19 USPQ 2d 1111, CAFC 1991, see also *In re Winkhaus*, 188 USPQ 129, CCPA 1975.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2 and 25-30 as amended now are rejected under 35 U.S.C. 102(e) as being anticipated by Olney (US 5925634) of record stated in the Office Action dated January 12, 2005.

Olney discloses that ibogaine alone or in absence of an opioid analgesic is useful in treating neuropathic pain wherein ibogaine is the sole agent for alleviating pain. See the title, abstract, col.7 lines 16-18; claim 1. Olney also discloses the range of the dose about 1-50 mg/kg per day or about 5-100 mg/kg/day which touch or overlap with the claimed range herein (see col.15 lines 35-38), and various administration routes, e.g., orally (see col.14-15).

Given the fact that noribogaine is a known metabolite of ibogaine (noribogaine is known to be 10-Hydroxyibogamine, a de-methyl-ibogaine; ibogaine is 10-methoxyibogamine), as Applicant admits and acknowledges regarding the prior art in the specification (see page 3), noribogaine was necessarily produced in the patient's body upon ingestion of ibogaine by hydrolysis in the body. Note that the court ruled that the metabolite of loratadine called descarboethoxyloratadine or "DCL" was INHERENTLY anticipated by loratadine (Claritin ™) because it was necessarily

produced in the patient's body upon ingestion of Claritin ™. See Schering Corp. v. Geneva Pharmaceuticals, Inc., 68 USPQ2d 1760 (CAFC 2003).

Note that Olney discloses that "neuropathic pain (i.e. pain which does not respond conventionally to opiate drugs such as morphine)" (emphasis added, see abstract and col.7 lines 16-18). Nonetheless, the pain which does not respond conventionally to opiate drugs such as morphine, does not limited the method of Olney to treat the pain which is not *treatable* with **any** opioid agonist analgesic.

Further, the recitation "without addition" is deemed an inherent property of noribogaine or ibogaine, and thus not a limitation to the claimed method.

Furthermore, Olney discloses that ibogaine can be used in combination with additional drugs (see col.7 line 27-32) which are not opioid analgesic agents.

Thus, Olney's method anticipates the claimed method.

Response to Argument

Applicant's arguments filed July 13, 2005 with respect to this rejection made under 35 U.S.C. 102(e) in the previous Office have been fully considered but they are not deemed persuasive to render the claimed invention patentable over the prior art. The remarks regarding the new limitation "pain treatable with an opioid agonist analgesic" has been discussed above.

Further, Applicant asserts that "Olney recognized (as the art recognized), that ibogaine did not act at the receptors at which opioid agonists acted (i.e., μ receptors). Rather, Olney teaches the use of ibogaine to treat neuropathic pain which is mediated through NMDA receptors by functioning as an antagonist of the NMDA receptor.

Because the present claims are directed to the treatment of pain mediated through μ receptors, not NMDA receptors, no anticipation of the present invention by Olney is made out."

However, whether ibogaine acts at the receptors at which opioid agonists acted (i.e., μ receptors) or not, or as an antagonist of the NMDA receptor, is considered a mere mechanism of action of ibogaine. Note that a mechanism of action of a treatment would not by itself carry patentable weight if the prior art teaches the same or nearly the same method steps. Applicant's recitation of a new mechanism of action for the prior art method will not, by itself, distinguish the instant claims over the prior art teaching the same or nearly the same method steps.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 102. Therefore, said rejection is adhered to.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Olney (US 5925634) or GB 841,697 (of record) in view of Hussain (4,464,378) and

Applicant's admission regarding the prior art in the specification (see page 1-3) of record stated in the Office Action dated January 12, 2005.

The same disclosure of Olney has been discussed in the 102(e) rejection set forth above.

GB 841,697 discloses that ibogaine is an analgesic agent, and is therefore useful in an analgesic composition for treating or alleviating pain. The effective amount or dose of ibogaine, 20-40 mg, is also taught in GB 841,697. See abstract, col.1-2, and claims 1-5.

The prior art does not expressly disclose the employment of noribogaine in combination with an opioid antagonist such as naloxone, naltrexone and nalorphine in a method of treating a patient to alleviate pain. The prior art does also not expressly disclose the particular effective amounts of naloxone, naltrexone and nalorphine to be administered with noribogaine in the claimed method.

Hussain teaches that opioid antagonists such as naloxone, naltrexone and nalorphine are well known analgesics and therefore useful in a method of treating or alleviating pain in a patient. See col.1 lines 44 and 56-57, col.3 lines 24-27, and claims 1-2.

Applicant's admission regarding the prior art in the specification (see page 3) teaches that noribogaine is a known metabolite of ibogaine and opioid antagonists such as naloxone, naltrexone and nalorphine are known analgesics and useful in a method of treating or alleviating pain in a patient.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ noribogaine in combination with an opioid antagonist such as naloxone, naltrexone and nalorphine in a method of treating a patient to alleviate pain, and to optimize the effective amounts of active agents in the composition herein to be administered.

One having ordinary skill in the art at the time the invention was made would have been motivated to employ noribogaine in combination with an opioid antagonist such as naloxone, naltrexone and nalorphine in a method of treating a patient to alleviate pain since opioid antagonists such as naloxone, naltrexone and nalorphine are well known to be useful in a method of treating a patient to alleviate pain.

Therefore, one of ordinary skill in the art would have reasonably expected that combining noribogaine and an opioid antagonist herein known useful for the same purpose (i.e., treating a patient to alleviate pain) in a composition to be administered would improve the therapeutic effect for alleviating pain.

Moreover, the combination of ibogaine and additional drugs taught by Olney is seen to provide the motivation for the combination claimed herein.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active ingredients in the composition because the effective amounts of noribogaine and an opioid antagonist herein are known in the art. In addition, the optimization of amounts of active agents to be administered is considered well within the skill of artisan.

Since all active composition components herein are known to useful to treat a patient to alleviate pain, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Response to Argument

Applicant's arguments filed January 12, 2005 with respect to the rejection made under 35 U.S.C. 103(a) in the previous Office Action January 12, 2005 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

The remarks regarding the new limitation "pain treatable with an opioid agonist analgesic" are believed to be adequately addressed above in the 102 rejection.

Applicant argues that "none of these references alone or in combination teaches or suggests the present invention and the present invention is non-obvious over the disclosure of these references."

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145. Moreover, it has been held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for same purpose in order to form a third composition that is to be used for the very same purpose; idea of combining them flows logically from their having been individually

taught in prior art. *In re Kerkhoven*, 205 USPQ 1069, CCPA 1980. See MPEP 2144.06. In the instant case, as discussed in the set forth 103(a) rejection, noribogaine or ibogaine is known to be used for treating pain; opioid antagonists such as naloxone, naltrexone and nalorphine are well known to be useful in a method of treating a patient to alleviate pain.

Therefore, one of ordinary skill in the art would have reasonably expected that combining noribogaine and an opioid antagonist herein known useful for the same purpose (i.e., treating a patient to alleviate pain) in a composition to be administered would improve the therapeutic effect for alleviating pain.

Moreover, the combination of ibogaine and additional drugs taught by Olney is seen to provide the motivation for the combination claimed herein.

Note that arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., In re Huang, 100 F.3d 135,139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); In re De Blauwe, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984). The burden is shifted to Applicant to show factually supported objective evidence to rebut the prima facie case of obviousness over the prior art.

In view of the rejections to the pending claims set forth above, no claims are allowed.

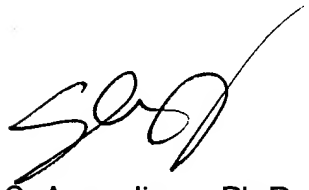
Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
September 21, 2005